Texas Medicaid/CHIP Vendor Drug Program
Drug Utilization Criteria For Outpatient Use Guidelines
Proton Pump Inhibitors

About
Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

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1. Dosage [*]
Proton pump inhibitors (PPIs) are FDA-approved for managing duodenal and gastric ulcers, erosive esophagitis (EE), gastroesophageal reflux disease (GERD), hypersecretory conditions, and heartburn, preventing nonsteroidal anti-inflammatory drug (NSAID)-induced ulcers, and eradicating *Helicobacter pylori* (as a component of combination therapy).

Omeprazole/sodium bicarbonate combination therapy is FDA-approved for managing gastric and duodenal ulcer, EE, GERD, and upper gastrointestinal bleed risk reduction in critically ill patients.

Esomeprazole combined with naproxen is FDA-approved for use in osteoarthritis (OA), rheumatoid arthritis (RA), or ankylosing spondylitis (AS) in adult patients at greater risk for developing NSAID-induced gastric ulcers.

Adults
Maximum daily adult doses for PPIs when prescribed as acute and maintenance therapy, as well as components of combination treatments, are summarized in Tables 1 and 2. Dosages exceeding these recommended values will be reviewed.

Table 1: Adult Maximum Daily Acute Dose for Proton Pump Inhibitors	
Drug Name	**Maximum Recommended Dosage**
Monotherapy	
dexlansoprazole (Dexilant®)	• EE: 60 mg/day • GERD (nonerosive): 30 mg/day
esomeprazole (Nexium®, generics)	• EE: 40 mg/day • GERD (nonerosive): 20 mg/day • *H. pylori* eradication: 40 mg/day • heartburn: 20 mg/day • hypersecretory conditions: 240 mg/day
lansoprazole (Prevacid®, generics)	• duodenal ulcer, GERD (nonerosive): 15 mg/day • EE, gastric ulcer, NSAID-associated gastric ulcer: 30 mg/day • heartburn (OTC*): 15 mg/day • *H. pylori* eradication: 90 mg/day (in divided doses) • hypersecretory conditions: 180 mg/day

omeprazole (Prilosec®, generics)	• duodenal ulcer, EE, GERD (nonerosive): 20 mg/day
	• gastric ulcer: 40 mg/day
	• heartburn (OTC): 20 mg/day
	• *H. pylori* eradication:
	  ○ triple therapy – 40 mg/day in divided doses
	  ○ dual therapy – 40 mg/day
	• hypersecretory conditions: 360 mg/day

pantoprazole (Protonix®, generics)	• EE: 40 mg/day • hypersecretory conditions: 240 mg/day
rabeprazole (Aciphex®, generics)	• duodenal ulcer, EE, GERD (nonerosive): 20 mg/day • *H. pylori* eradication: 40 mg/day **(in divided doses)** • hypersecretory conditions: 120 mg/day (in divided doses)
Combination Therapy	
omeprazole/sodium bicarbonate (Zegerid®, generics)	• duodenal ulcer, EE, GERD (nonerosive): 20 mg/day • gastric ulcer: 40 mg/day • heartburn (OTC): 20 mg/day • upper GI bleed risk reduction in critically ill (suspension only): 40 mg/day

**over-the-counter*

Table 2: Adult Maximum Daily Maintenance Dose for Proton Pump Inhibitors	
Drug Name	**Maximum Recommended Dosage**
Monotherapy	
dexlansoprazole	• EE: 30 mg/day • **heartburn: 30 mg/day**
esomeprazole	• EE: 20 mg/day • hypersecretory conditions: 240 mg/day • risk reduction of NSAID-associated gastric ulcer: 40 mg/day
lansoprazole	• duodenal ulcer, EE: 15 mg/day • hypersecretory conditions: 180 mg/day • risk reduction of NSAID-associated gastric ulcer: 15 mg/day
omeprazole	• EE: 20 mg/day • hypersecretory conditions: 360 mg/day
pantoprazole	• EE: 40 mg/day • hypersecretory conditions: 240 mg/day
rabeprazole	• EE: 20 mg/day • hypersecretory conditions: 120 mg/day (in divided doses)
Combination Therapy	
esomeprazole/naproxen (Vimovo®)	• prevention of NSAID-associated gastric ulcer in patients with OA, RA, AS: 40 mg/1000 mg per day

Pediatrics
Safety and efficacy of dexlansoprazole in patients less than 12 years of age as well as omeprazole/sodium bicarbonate and esomeprazole/naproxen in patients less than 18 years of age have not been established.

Esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole are FDA-approved for use in pediatric patients; doses are age-dependent. The maximum recommended daily pediatric doses for these PPIs are summarized in Table 3. Dosages exceeding these recommendations will be reviewed.

Table 3: Pediatric Maximum Recommended Doses for Proton Pump Inhibitors	
Drug Name	**Maximum Recommended Dosage**
dexlansoprazole	**acute therapy:** ***12 to 17 years of age:*** • **EE: 60 mg/day** • **GERD: 30 mg/day** **maintenance therapy:** • **heartburn: 30 mg/day**

Table 3: Pediatric Maximum Recommended Doses for Proton Pump Inhibitors (continued)	
Drug Name	**Maximum Recommended Dosage**
esomeprazole	acute therapy: *1 to 11 months of age:* • EE due to only acid-mediated GERD: ○ 3 kg to 5 kg: 2.5 mg once daily ○ 5 kg to 7.5 kg: 5 mg once daily ○ 7.5 kg to 12 kg: 10 mg once daily *1 to 11 years of age:* • EE: ○ 20 kg: 20 mg/day ○ < 20 kg: 10 mg/day • GERD: 10 mg/day *12 to 17 years of age:* • EE: 40 mg/day • GERD: 20 mg/day
lansoprazole	acute therapy: *1 to 11 years of age:* • GERD, EE*: ○ 30 kg: 30 mg/day ○ < 30 kg: 15 mg/day *≥ 12 years of age:* • EE: 30 mg/day • GERD: 15 mg/day
omeprazole	acute therapy: **1 month to < 1 year of age:** • **EE:** ○ **3 to < 5 kg: 2.5 mg /day** ○ **5 to < 10 kg: 5 mg/day** ○ **≥ 10 kg: 10 mg/day** ***1 to 16 years of age:*** • EE, GERD: ○ 5 to < 10 kg: 5 mg /day ○ 10 to < 20 kg: 10 mg/day ○ ≥ 20 kg: 20 mg/day
pantoprazole	acute therapy: *≥ 5 years of age:* • EE: ○ 15 kg to < 40 kg: 20 mg/day ○ ≥ 40 kg: 40 mg/day
rabeprazole	acute therapy: *1 to 11 years of age:* • GERD: ○ < 15 kg: 5 mg once daily+ ○ ≥ 15 kg: 10 mg once daily *≥ 12 years of age:* • GERD: 20 mg once daily

**dose increased to 30 mg twice daily in some children who remained symptomatic after 2 weeks of therapy at lower doses*
+may increase to 10 mg daily in those with inadequate response to 5 mg dose

Although not FDA-approved due to limited availability of guidelines and well-designed clinical trials, select proton pump inhibitors have been utilized in combination with antibiotic therapy to manage *H. pylori* in pediatric patients. The 2011 European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guidelines for *H. pylori* management in pediatric patients recommend PPI doses of 1-2 mg/kg/day for 10 to 14 days as combination therapy or sequential therapy. Pediatric dosage recommendations for *H. pylori* management are summarized in Table 4.

Table 4: ESPGHAN/NASPGHAN Pediatric *H. pylori* Treatment Recommendations

Treatment Option	Oral Dosage
Option 1: amoxicillin clarithromycin PPI	 50 mg/kg/day up to 1 g twice daily 20 mg/kg/day up to 500 mg twice daily 1-2 mg/kg/day
Option 2: amoxicillin metronidazole PPI	 50 mg/kg/day up to 1 g twice daily 20 mg/kg/day up to 500 mg twice daily 1-2 mg/kg/day
Option 3: **bismuth salts** **amoxicillin** **metronidazole**	 **8 mg/kg/day** **50 mg/kg/day (max, 2 g/day)** **20 mg/kg/day (max, 1 g/day)**
Sequential therapy*: PPI + amoxicillin *followed by* PPI + metronidazole + clarithromycin	 1-2 mg/kg/day 50 mg/kg/day up to 1 g twice daily 1-2 mg/kg/day 20 mg/kg/day 20 mg/kg/day up to 500 mg twice daily

**sequential therapy = PPI + amoxicillin x 5 days followed by PPI + metronidazole + clarithromycin x 5 days*

Dosage in Renal Impairment
Dosage adjustments are not necessary when PPIs are prescribed as monotherapy to patients with renal impairment. Omeprazole/sodium bicarbonate therapy also does not require dosage adjustments in renally impaired patients. However, the esomeprazole/naproxen combination is not recommended for use in patients with a creatinine clearance below 30 ml/min due to the potential for naproxen/naproxen metabolite accumulation and increased risk for adverse events.

2. **Duration of Therapy**
PPI acute treatment durations for both adult and pediatric patients based on FDA-approved indications are summarized in Table 5.

Table 5: PPI Acute Duration of Therapy for Adult and Pediatric Patients		
Drug	**Maximum Recommended Treatment Duration (based on FDA-approved indication)**	
	Indication	**Duration**
Adults: Monotherapy		
dexlansoprazole	EE GERD	8 weeks 4 weeks
esomeprazole	EE GERD heartburn	8 weeks^ 4 weeks+ 14 days*
lansoprazole	duodenal ulcer EE gastric ulcer, GERD heartburn NSAID-associated gastric ulcer -without prior gastric ulcer -with prior gastric ulcer	4 weeks 8 weeks# 8 weeks 14 days* 8 weeks 12 weeks
omeprazole	duodenal ulcer EE gastric ulcer GERD Heartburn	4 weeks+ 8 weeks# 8 weeks 4 weeks 14 days*
pantoprazole	EE	8 weeks#
rabeprazole	duodenal ulcer EE GERD	4 weeks+ 8 weeks# 4 weeks+
Adults: Combination Therapy		
omeprazole/sodium bicarbonate	duodenal ulcer EE gastric ulcer GERD (nonerosive) heartburn upper GI bleed risk reduction in critically ill	4 weeks+ 8 weeks# 8 weeks 4 weeks 14 days* 14 days~
Pediatrics: Monotherapy		
dexlansoprazole	***12 to 17 years of age:*** **EE**	 **8 weeks**
esomeprazole	*1 to 11 months of age:* EE due to acid-mediated GERD *1 to 11 years of age:* EE healing, symptomatic GERD *12 to 17 years of age:* EE healing symptomatic GERD	 6 weeks 8 weeks 8 weeks 4 weeks
lansoprazole	*1 to 11 years of age:* EE, GERD *12 to 17 years of age:* EE, GERD	 12 weeks 8 weeks

Table 5: PPI Acute Duration of Therapy for Adult and Pediatric Patients (continued)		
Drug	**Maximum Recommended Treatment Duration (based on FDA-approved indication)**	
	Indication	Duration
Pediatrics: Monotherapy (continued)		
omeprazole	***1 month to < 1 year of age:*** **EE** ***1 to 16 years of age:*** **EE**	**6 weeks** **12 weeks∞**
pantoprazole	*≥ 5 years of age:* EE	8 weeks
rabeprazole	*1 to 11 years of age:* GERD *12 to 17 years of age:* GERD	12 weeks 8 weeks

^may consider an additional 4- to 8-week treatment course in patients who do not heal with initial treatment
+may consider an additional 4-week treatment course in patients who do not heal with initial treatment
#may consider an additional 8-week treatment course in patients with incomplete healing or EE recurrence after initial treatment
** PPI treatment duration should not exceed 14 days during a 4-month period, unless alternate instructions are provided by a physician*
~ treatment longer than 14 days has not been studied in critically ill patients
∞may consider additional 4- to 8-week treatment course with EE or GERD recurrence

In the acute setting in both adult and pediatric patients older than 11 months of age, 8 weeks of PPI therapy will treat EE and will heal most non-*H. pylori* duodenal and gastric ulcers. The prescribing health care provider may continue acute dosage regimens for longer than 8 weeks in patients with hypersecretory disease states, esophagitis, or GERD, as well as those patients with risk factors for gastric ulcer treatment failure such as smoking. PPI acute dosage regimens may also exceed 8 weeks in patients with risk factors for delayed duodenal ulcer healing such as daily ethanol use, large ulcers, signs of upper GI bleeding, and/or a previous history of duodenal ulcer. Patients with refractory ulcers, defined as ulcers that do not respond to up to 12 weeks of anti-ulcer therapy, may also require extended PPI therapy. Treatment regimens at acute dosage levels lasting longer than four months (16 weeks) in patients with a diagnosis of acute duodenal or gastric ulcer will be reviewed.

Clinical trials support dexlansoprazole efficacy for maintenance of healed EE and heartburn relief for up to six months in adults and up to 16 weeks in pediatric patients 12 to 17 years of age.

Esomeprazole, when prescribed for risk reduction of NSAID-associated gastric ulcer, may be administered For up to six months, as controlled studies for this indication do not extend beyond this time period. Treatment regimens for NSAID-associated gastric ulcers extending beyond designated treatment times for Esomeprazole and lansoprazole will be reviewed.

Unless otherwise specified, maintenance therapy, at the recommended daily maintenance dose (Tables 2 and 3), may be continued indefinitely based on patient need. Omeprazole treatment for EE and GERD in pediatric patients may continue indefinitely.

PPI treatment duration in adults for *H. pylori* eradication is summarized in Table 6. PPI therapy is prescribed for a maximum of 14 days in most patients, as treatment durations exceeding 14 days do not significantly increase eradication rates. In treatment failures, retreatment with an alternate antibiotic regimen has been beneficial. In these circumstances, patients may receive PPI therapy for a maximum of 28 days.

Table 6: Proton Pump Inhibitor Recommended Therapy Duration in Adults for *H. pylori* Eradication	
Drug	**Recommended Therapy Duration**
esomeprazole	with triple therapy: 10 days
lansoprazole	with dual therapy: 14 days with triple therapy: 10-14 days
omeprazole	with ulcer present at treatment initiation, dual or triple therapy: 28 days without ulcer present at treatment initiation, dual therapy: 14 days triple therapy: 10 days
rabeprazole	with triple therapy: 7 days

Pediatric treatment regimens for *H. pylori* eradication reported in guidelines and clinical trials should be administered for 10 to 14 days. Pediatric sequential therapy for H. pylori eradication is comprised of a PPI plus amoxicillin administered for 5 days, followed by a PPI plus metronidazole plus clarithromycin given for 5 days.

3.* **Duplicative Therapy**
The combination of two or more PPIs is not supported by the current literature. Additional clinical benefit is not realized when multiple PPIs are prescribed adjunctively. Therefore, concurrent use of multiple PPIs will be reviewed.

4.* **Drug-Drug Interactions**
Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for PPIs are summarized in Table 7. Only those drug-drug interactions identified as clinical significance level 1 or contraindicated, or those considered life-threatening which have not yet been classified will be reviewed:

Table 7: Major PPI Drug-Drug Interactions				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance*+**
dexlansoprazole, esomeprazole, lansoprazole, omeprazole	**tacrolimus**	**adjunctive administration may result in increased tacrolimus serum levels as tacrolimus is metabolized by CYP3A4, and select PPIs are substrates for CYP3A4 and CYP2C19**	**Avoid combination, if possible; if concurrent therapy necessary, monitor serum tacrolimus levels and observe for adverse events; adjust doses as needed**	**major, moderate (DrugReax) 3-moderate (CP)**
esomeprazole, omeprazole	cilostazol (Pletal®)	adjunctive use may increase cilostazol serum levels and enhance cilostazol pharmacologic/adverse effects as cilostazol is metabolized by CYP2C19 as esomeprazole and omeprazole are CYP2C19 inhibitors	reduce cilostazol dose by 50% when given concurrently with omeprazole and monitor for enhanced cilostazol pharmacologic/adverse effects	moderate (DrugReax) 2-major (CP)
esomeprazole, omeprazole	citalopram (Celexa®)	adjunctive use may increase citalopram serum levels and enhance citalopram, pharmacologic/adverse effects (including QT interval prolongation) as citalopram is metabolized by CYP2C19 and esomeprazole and omeprazole are CYP2C19 inhibitors	citalopram dose should not exceed 20 mg/day if this drug combination is utilized; monitor for enhanced citalopram pharmacologic/adverse effects	major (DrugReax) 2-major (CP)
esomeprazole, omeprazole, pantoprazole	methotrexate (MTX)	concurrent administration of select PPIs and MTX (primarily high-dose MTX) may result in elevated MTX parent and metabolite concentrations and the potential for enhanced pharmacologic and adverse effects; these PPIs reduce renal MTX elimination	use combination cautiously; monitor MTX levels and observe patients for signs/symptoms of adverse events; may use alternative PPI or H2RA that does not interact; may not occur with lower MTX doses	major (DrugReax) 2-major (CP)

Table 7: Major PPI Drug-Drug Interactions (continued)				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance*+**
PPIs	select azole antifungals (e.g., itraconazole, ketoconazole, posaconazole)	combined administration may decrease antifungal absorption and effectiveness; itraconazole, ketoconazole, and posaconazole dependent on acidic environment for favorable absorption and PPIs increase gastric pH	avoid concurrent administration, if possible; if PPI-antifungal combination necessary, may administer antifungal with acidic beverage (e.g., Coke) to increase absorption; monitor closely for continued antifungal efficacy	moderate (DrugReax) 2-major (CP)
PPIs	clopidogrel (Plavix®)	combined administration may attenuate clopidogrel effects on platelet aggregation, increase potential risk of secondary acute cardiovascular events following percutaneous coronary intervention or acute coronary syndrome; exact mechanism for interaction unknown, but PPIs may delay or minimize clopidogrel conversion to its active form by competitively inhibiting CYP2C19	avoid combined use, if possible; H2RAs# other than cimetidine or pantoprazole (has less CYP2C19 inhibitory activity) are suitable alternatives for acid suppressive therapy in patients requiring clopidogrel	major (DrugReax) 2-major (CP)
PPIs	dasatinib (Sprycel®)	adjunctive administration for extended duration may result in reduced dasatinib exposure and serum levels as dasatinib dependent on acidic gastric pH for solubility and absorption	combined use not recommended; alternative acid suppressives (e.g., antacids) should be given 2 hours before or 2 hours after dasatinib dose for optimal efficacy	major (DrugReax) 2-major (CP)
PPIs	delavirdine	combined use for extended treatment duration may result in reduced delavirdine absorption, decreased delavirdine serum levels, and attenuated delavirdine efficacy as delavirdine is dependent on an acidic gastric pH for absorption; separating drug doses may not improve delavirdine absorption as PPIs affect gastric pH for prolonged time period	concomitant use not recommended; antacids may be alternative acid suppressive therapy, with antacid and delavirdine doses separated by at least one hour	major (DrugReax) 2-major (CP)

Table 7: Major PPI Drug-Drug Interactions (continued)				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance***
PPIs	erlotinib (Tarceva®)	adjunctive administration may decrease erlotinib absorption and reduce effectiveness as erlotinib solubility, which is pH dependent, is reduced with PPI therapy	avoid combination, if possible; if adjunctive therapy necessary, use lowest effective PPI dose, monitor for reduced erlotinib efficacy, and adjust erlotinib dose as needed; may use alternate acid suppressive therapy (e.g., H2RAs, antacids); antacid and erlotinib doses should be separated by several hours	major (DrugReax)
PPIs	mycophenolate	combined administration may result in decreased mycophenolic acid serum levels and reduced therapeutic efficacy, most likely due to decreased mycophenolate absorption with increased gastric pH	avoid combined use, if possible; if adjunctive therapy necessary, closely monitor mycophenolic acid serum levels and adjust mycophenolate doses as necessary	major (DrugReax)
PPIs	select protease inhibitors (e.g., atazanavir, indinavir, nelfinavir)	concurrent administration may result in reduced protease inhibitor serum levels and effectiveness and increased potential for resistance, as PPIs may interfere with protease inhibitor solubility and absorption by increasing gastric pH	avoid PPI and atazanavir, indinavir, or nelfinavir combinations	major (DrugReax) 1-severe: atazanavir, nelfinavir; 2-major: indinavir (CP)
PPIs	rilpivirine (Edurant®)	adjunctive administration may promote rilpivirine treatment failure and potential for impaired virologic response and rilpivirine/NNRI† resistance as rilpivirine requires more acidic gastric pH for absorption	combined administration contraindicated	contraindicated (DrugReax) 1-severe (CP)

Table 7: Major PPI Drug-Drug Interactions (continued)				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance***
PPIs	other agents with solubility affected by changes in gastric pH (e.g., bosutinib, ponatinib, vismodegib)	concomitant administration may result in reduced bioavailability and activity of agents requiring low gastric pH for solubility as PPIs increase gastric pH	avoid combination, if possible; if adjunctive therapy necessary, use lowest effective PPI dose, monitor for reduced efficacy of agents requiring low gastric pH for solubility, and adjust dose as needed; may use alternate acid suppressive therapy (e.g., H2RAs, antacids); antacid and doses for agents with solubility issues should be separated by several hours	major (DrugReax)
PPIs	**vitamin K antagonists (e.g., warfarin)**	**concurrent administration may result in elevated INR^ levels and prothrombin time and enhanced anticoagulant effects; warfarin is metabolized by CYP2C19 and omeprazole is a CYP2C19 inhibitor, but mechanism for other PPIs is not well known**	**monitor INR levels and observe for bleeding issues/adverse effects; adjust warfarin doses as needed**	**moderate (DrugReax) 3-moderate (CP)**

**CP = Clinical Pharmacology*
#histamine (H2) receptor antagonists †non-nucleoside reverse transcriptase inhibitor ***^International Normalized Ratio***

REFERENCES

1. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com.libproxy.uthscsa.edu. **Accessed December 4th, 2016.**
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; **2016.** Available at: http://www.clinicalpharmacology.com. **Accessed December 4th, 2016.**
3. **Facts and Comparisons eAnswers [database online]. Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.;2016. Available at: http://eanswers.factsandcomparisons.com.ezproxy.lib.utexas.edu/. Accessed December 4th, 2016.**
4. **AHFS Drug Information 2016.** Jackson, WY: Teton Data Systems, **Version 8.8.1, 2015.** Stat!Ref Electronic Medical Library. Available at: http://online.statref.com.libproxy.uthscsa.edu/. **Accessed December 4th, 2016.**
5. Esomeprazole (Nexium®) package insert. AstraZeneca Pharmaceuticals LP, **October 2016.**
6. Omeprazole (Prilosec®) package insert. AstraZeneca Pharmaceuticals LP, **March 2014.**
7. Lansoprazole (Prevacid®) package insert. Takeda Pharmaceuticals America, Inc., **October 2016.**
8. Pantoprazole (Protonix®) package insert. Pfizer, **October 2016.**
9. Naproxen/esomeprazole (Vimovo®) package insert. Horizon Pharma USA Inc., **October 2016.**
10. Omeprazole/sodium bicarbonate (Zegerid®) package insert. Salix Pharmaceuticals, Inc., **June 2016.**
11. **Dexlansoprazole (Dexilant®) package insert. Takeda Pharmaceuticals America, Inc., October 2016.**
12. Koletzko S, Jones NL, Goodman KJ, et al, on behalf of the *H. pylori* working groups of ESPGHAN and NASGHAN. Evidence-based guidelines from ESPGHAN and NASPGHAN for Helicobacter pylori infection in children. J Pediatr Gastroenterol Nutr. 2011;53:230-43.
13. **Ertem D. Clinical practice: Helicobacter pylori infection in childhood. Eur J Pediatr. 2013;172(11):1427-34.**
14. Atazanavir (Reyataz®) package insert. Bristol-Myers Squibb, **September 2016.**
15. Walan A, Bader JP, Classen M, et al. Effect of omeprazole and ranitidine on ulcer healing and relapse rates in patients with benign gastric ulcer. N Engl J Med. 1989;320:69-75.
16. Van Der Meer JWM, Keuning JJ. The influence of gastric acidity on the bioavailability of ketoconazole. J Antimicrob Chemother. 1980;6:552-4.
17. Graham DY, Agrawal NM, Campbell DR, et al. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of misoprostol vs lansoprazole. Arch Intern Med. 2002;162:169-75.
18. Kahrilas PJ. Gastroesophageal reflux disease. N Engl J Med. 2008;359(16):1700-7.
19. Chey WD, Wong BCY, and the Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. 2007;102:1808-25.
20. Lazzaroni M, Porro GB. Management of NSAID-induced gastrointestinal toxicity: focus on proton pump inhibitors. Drugs. 2009;69(1):51-69.
21. Shi S, Klotz U. Proton pump inhibitors: an update of their clinical use and pharmacokinetics. Eur J Clin Pharmacol. 2008;64(10):935-51.
22. Shashidhar H, Peters J, Lin CH, et al. A prospective trial of lansoprazole triple therapy for pediatric Helicobacter pylori infection. J Pediatr Gastroenterol Nutr. 2000;30:276-82.
23. Behrens R, Lang T, Keller KM, et al. Dual versus triple therapy of Helicobacter pylori infection: results of a multicentre trial. Arch Dis Child. 1999;81:68-70.
24. Zimmermann AE, Walters JK, Katona BG, et al. A review of omeprazole use in the treatment of acid-related disorders in children. Clin Ther. 2001;23:660-79.
25. Marchetti F, Gerarduzzi T, Ventura A. Proton pump inhibitors in children: a review. Dig Liver Dis. 2003;35:738-46.

26. Kahrilas PJ, Shaheen NJ, Vaezi MF, for the AGA Institute. American Gastroenterological Association medical position statement on the management of gastroesophageal reflux disease. Gastroenterology. 2008;135:1383-91.
27. **van der Pol RJ, Smits MJ, van Wijk MP, et al. Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review. Pediatrics. 2011;127(5):925-35.**
28. Wolfe WM. Overview and comparison of the proton pump inhibitors for the treatment of acid-related disorders In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. **(Accessed on December 4th, 2016.)**
29. Crowe SE. Treatment regimens for *Helicobacter pylori*. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. **(Accessed on December 4th, 2016.)**
30. Love BL, Thoma MN. Chapter 20. Peptic ulcer disease. (Chapter) In: DiPiro JT, Talbert RL, Yee GC, et al. (eds): Pharmacotherapy: a pathophysiologic approach. 9th edition. New York, McGraw-Hill, 2014. Access Pharmacy Web site. Available at: http://www.accesspharmacy.com.ezproxy.lib.utexas.edu. **Accessed December 4th, 2016.**
31. DRUG-REAX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.thomsonhc.com.libproxy.uthscsa.edu. **Accessed December 4th, 2016.**

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